

DOCKET NO.: CELL-0307/PA534-USW01  
PATENT



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of:

David Paul Humphreys, et al.

Application No.: 10/562,807

Filing Date: July 6, 2006

For: MODIFIED ANTIBODY FRAGMENTS

Confirmation No.: 6569

Group Art Unit: Not Yet Assigned

Examiner: Not Yet Assigned

DATE OF DEPOSIT:

*October 6, 2006*

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*Elizabeth A. McLoud*

TYPED NAME: Elizabeth A. McLoud

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Dear Sir:

### INFORMATION DISCLOSURE STATEMENT

Pursuant to 37 CFR § 1.56 and in accordance with 37 CFR §§ 1.97-1.98, information relating to the above-identified application is hereby disclosed. Inclusion of information in this statement is not to be construed as an admission that this information is material as that term is defined in 37 CFR § 1.56(b).

- ☒ In accordance with § 1.97(b), since this Information Disclosure Statement is being filed either within three months of the filing date of the above-identified application, within three months of the date of entry into the national stage of

the above identified application as set forth in § 1.491, before the mailing date of a first Office Action on the merits of the above-identified application, or before the mailing date of a first Office Action after the filing of request for continued examination under § 1.114, no additional fee is required.

- ☐ In accordance with § 1.97(c), this Information Disclosure Statement is being filed after the period set forth in § 1.97(b) above but before the mailing date of either a Final Action under § 1.116 or a Notice of Allowance under § 1.311, or before an action that otherwise closes prosecution in the application, therefore:

☐ Certification in Accordance with § 1.97(e) is attached; or

☐ The fee of \$180.00 as set forth in § 1.17(p) is attached.

- ☐ In accordance with § 1.97(d), this Information Disclosure Statement is being filed after the mailing date of either a Final Action under § 1.113 or a Notice of Allowance under § 1.311 but before, or simultaneously with, the payment of the Issue Fee, therefore included are: Certification in Accordance with § 1.97(e); and the submission fee of \$180.00 as set forth in § 1.17(p).

- ☒ Copies of reference numbers 1 – 26 and 34 - 46 listed on the attached Form PTO-1449 are enclosed herewith.

- ☒ Copies of reference numbers 27 - 33 on the attached Form PTO 1449 are not required to be submitted pursuant to 37 CFR § 1.98(a)(2)(i).

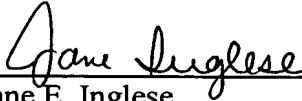
- ☐ Copies of references - are not being submitted because they were previously cited by or submitted to the U.S. Patent and Trademark Office in patent application number , filed for which a claim for priority under 35 U.S.C. § 120 has been made in the instant application.

☐ The relevance of those listed references which are not in the English language is as follows:

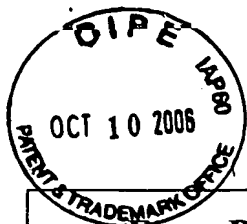
There are no listed references which are not in the English language.

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Date: *October 6, 2006*

  
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<b>Form PTO-1449 Modified</b>  List of Patent and Publications Cited by Applicant (Use several sheets if necessary)  U.S. Department of Commerce Patent and Trademark Office		Docket No. CELL-0307/PA534-USw01	Application No. 10/562,807
		Applicant David Paul Humphreys, et al.	
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<b>NON-PATENT DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)</b>			
	1	Begg, et al., "Mass spectrometry detection and reduction of disulfide adducts between reducing agents and recombinant proteins with highly reactive cysteines," <i>J. of Biomolecular Techniques</i> , <b>1999</b> , 10, 17-20	
	2	Bird, R.E., et al., "Single-chain antigen-binding proteins," <i>Science</i> , <b>1988</b> , 242, 423	
	3	Burns, J., et al., "Selective reduction of disulfides by tris(2-carboxyethyl)phosphine," <i>J. Org. Chem.</i> , <b>1991</b> , 56, 2648-2650	
	4	Chapman, A.P., et al., "Therapeutic antibody fragments with prolonged in vivo half-lives," <i>Nature Biotechnology</i> , <b>1999</b> , 17, 780-783	
	5	Chapman, A.P., et al., "PEGylated antibodies and antibody fragments for improved therapy: a review," <i>Advanced Drug Delivery Reviews</i> , <b>2002</b> , 54, 531-545	
	6	Dubowchik, G.M., et al., "Receptor-mediated and enzyme-dependent targeting of cytotoxic anticancer drugs," <i>Pharmacology and Therapeutics</i> , <b>1999</b> , 83, 67-123	
	7	Ellison, D., et al., "Photoreduction of monoclonal antibodies for conjugation and fragmentation," <i>Biotechniques</i> , <b>2000</b> , 28(2), 324-326	
	8	Getz, E.B., et al., "A comparison between the sulfhydryl reductants tris(2-carboxyethyl)phosphine and dithiothreitol for use in protein biochemistry," <i>Analytical Biochemistry</i> , <b>1999</b> , 273, 73-80	
	9	Han, J.C., et al., "A procedure for quantitative determination of Tris(2-carboxyethyl)phosphine, an odorless reducing agent more stable and effective than dithiothreitol," <i>Analytical Biochemistry</i> , <b>1994</b> , 220, 5-10	
	10	Hellstrom, K.E., et al., "Antibodies for drug delivery," <i>Controlled Drug Delivery</i> , 2 <sup>nd</sup> Ed., Robinson, et al. (Eds.), <b>1987</b> , 623-653	
	11	Humphreys, D.P., et al., "Formation of dimeric fabs in <i>Escherichia coli</i> : effect of hinge size and isotype, presence of interchain disulphide bond, Fab' expression levels, tail piece sequences and growth conditions," <i>J. of Immunological Methods</i> , <b>1997</b> , 209, 193-202	

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	12	Humphreys, D.P., et al., "A plasmid system for optimization of Fab' production in <i>Escherichia coli</i> : importance of balance of heavy chain and light chain synthesis," <i>Protein Expression and Purification</i> , <b>2002</b> , 26, 309-320	
	13	Humphreys, D.P., et al., "Efficient site specific removal of a C-terminal FLAG fusion from a Fab' using copper (II) ion catalysed protein cleavage," <i>Protein Engineering</i> , <b>1999</b> , 2, 179-184	
	14	Leach, S.J., et al., "The electrolytic reduction of proteins," <i>Div. Protein Chem.</i> , <b>1965</b> , 4, 23-27	
	15	Leong, S.R., et al., "Adapting pharmacokinetic properties of a humanized anti-interleukin-8 antibody for therapeutic applications using site-specific pegylation," <i>Cytokine</i> , <b>2001</b> , 16, 106-119	
	16	Lyons, A., et al., "Site-specific attachment to recombinant antibodies via introduced surface cysteine residues," <i>Protein Engineering</i> , <b>1990</b> , 3, 703-708	
	17	Mountain, A., et al., "Engineering antibodies for therapy," <i>Biotechnol. Genet. Eng. Rev.</i> , <b>1992</b> , 10, 1-142	
	18	Orlandi, R., et al., "Cloning immunoglobulin variable domains for expression by the polymerase chain reaction," <i>Proc. Natl. Acad. Sci. USA</i> , <b>1989</b> , 86, 3833-3837	
	19	Riechmann, L., et al., "Reshaping human antibodies for therapy," <i>Nature</i> , <b>1988</b> , 322, 323	
	20	Rodrigues, M.L., et al., "Engineering Fab' fragments for efficient F(ab) <sub>2</sub> formation in <i>Escherichia coli</i> and for improved in vivo stability," <i>The Journal of Immunology</i> , <b>1993</b> , 151, 6954-6961	
	21	Rüegg, U.T., et al., "Reduction cleavage of cystine disulfides with tributylphosphine," <i>Methods in Enzymology</i> , <b>1977</b> , 47, 111-126	
	22	Seitz, U., et al., "Preparation and evaluation of the rhenium-188-labelled anti-NCA antigen monoclonal antibody BW 250/183," <i>Euro. J. Nuclear Medicine</i> , <b>1999</b> , 26, 1265-1273	
	23	Singh, R., et al., "Reagents for rapid reduction of disulfide bonds," <i>Methods in Enzymology</i> , <b>1995</b> , 251, 167-173	
	24	Thorpe, P.E., et al., "The preparation and cytotoxic properties of antibody-toxin conjugates," <i>Immunol. Rev.</i> , <b>1982</b> , 62, 119-158	

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<b>NON-PATENT DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)</b>			
	25	Verma, R., et al., "Antibody engineering: comparison of bacterial, yeast, insect and mammalian expression systems," <i>J. of Immunological Methods</i> , <b>1998</b> , 216, 165-181	
	26	Ward, E., et al., "Binding activities of a repertoire of single immunoglobulin variable domains secreted from <i>Escherichia coli</i> ," <i>Nature</i> , <b>1989</b> , 341, 544-546	

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## U. S. PATENT DOCUMENTS

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### FOREIGN PATENT DOCUMENTS

Examiner Initial		Document No.	Date	Country	Translation	
					YES	NO
	34	WO 89/01476 A1	02/23/89	PCT		
	35	WO 90/09195 A1	08/23/90	PCT		
	36	WO 91/09967 A1	07/11/91	PCT		
	37	WO 92/02551 A1	02/20/92	PCT		
	38	WO 92/22583 A2	12/23/92	PCT		
	39	WO 93/06231 A1	04/01/93	PCT		
	40	WO 97/36932 A1	10/9/97	PCT		
	41	WO 98/25971 A1	06/18/98	PCT		
	42	WO 98/37200	08/27/98	PCT		
	43	WO 99/15549 A3	04/01/99	PCT		
	44	WO 03/031581 A3	04/17/03	PCT		
	45	1 419 786 A1	05/19/04	EP		
	46	3 927 45 B1	11/02/94	EP		

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